

### LISTING OF CLAIMS

1. *(currently amended)*: A method of killing melanoma cells comprising contacting said cells for an effective time with an effective amount of an organic small molecule inhibitor of MAPK/ERK kinase (MEK) enzymes which inhibitor

- (i) is a direct, noncompetitive inhibitor of MEK which does not inhibit the binding of the enzyme to one of its substrates, adenosine triphosphate (ATP); and
- (ii) induces apoptosis in said cells, thereby killing the cells,

wherein said inhibitor is PD98059 or PD184352.

2. *(withdrawn)* The method of claim 1, wherein said inhibitor is a MEK-directed protease.

3. *(withdrawn)* The method of claim 2, wherein said protease is *Bacillus anthracis* lethal factor or a functional derivative thereof.

#### **CANCEL Claim 4**

5. *(currently amended)*: The method of claim 1 [[4]] wherein said inhibitor is PD184352.

6. *(currently mended)*: The method of any of claims 1<sub>[[, 4]]</sub> or 5, wherein said contacting is *in vivo*.

7. *(original)*: The method of claim 6 wherein said killing results in measurable regression of melanoma tumor or attenuation of melanoma growth.

8. *(withdrawn)* A method of protecting against melanoma in a susceptible subject, comprising administering to said subject that is

- (a) at risk for development of melanoma or,
  - (b) in the case of an already treated subject, at risk for recurrence of melanoma,
- an effective amount of a MAPK-inhibitor.

9. *(currently amended)*: A method of inducing an antitumor response in a mammal having melanoma, comprising administering an effective amount of an organic small molecule inhibitor of MEK enzyme to said mammal, which inhibitor:

- (a) is a direct, noncompetitive inhibitor of MEK which does not inhibit the binding of the enzyme to one of its substrates ATP and is selected from the group consisting of PD98059 and PD184352; and
- (b) induces apoptosis in and is cytotoxic to melanoma cells in said mammal, thereby inducing an antitumor response that comprises
  - (i) at least a 50% decrease in tumor size measured as the sum of the products of maximal perpendicular diameters of all measurable lesions;
  - (ii) absence of new lesions, and
  - (iii) lack of progression of any preexisting lesions.

10. *(previously amended)*: The method of claim 9 wherein said antitumor response further comprises the disappearance of all evidence of melanoma disease for at least one month.

11. *(withdrawn)* The method of claim 9, wherein said inhibitor is a MEK-directed protease.

12. *(withdrawn)*. The method of claim 11, wherein said protease is *Bacillus anthracis* lethal factor or a functional derivative thereof.

### **CANCEL Claim 13**

14. *(currently amended)*: The method of claim 9 [[13]] wherein said inhibitor is PD184352.

15. *(currently amended)*: The method of any of claims 9, 10 [[, 13]] or 14, wherein said mammal is a human.

16. *(currently amended)*: A method of inhibiting growth or recurrent growth of a melanoma tumor in a mammal having melanoma or at risk for melanoma growth or recurrence, comprising administering to said mammal an effective amount of an organic small molecule inhibitor of MEK enzyme ~~to said mammal~~ selected from the group consisting of PD98059 and PD184352, said ~~inhibitor being a direct, noncompetitive inhibitor of MEK that does not inhibit the binding of the enzyme to one of its substrates, ATP,~~ thereby inducing a cytotoxic response leading to apoptosis of melanoma cells in said mammal, which response inhibits said growth or recurrent growth of said melanoma tumor.

17. *(withdrawn)* The method of claim 16 wherein said inhibitor is a MEK-directed protease.

18. *(withdrawn)* The method of claim 17, wherein said protease is *Bacillus anthracis* lethal factor or a functional derivative thereof.

#### **CANCEL Claim 19**

20 *(currently amended)*: The method of claim 16 ~~[[19]]~~ wherein said inhibitor is PD184352.

21 *(currently amended)*: The method of any of claims ~~16~~ ~~[[, 19]]~~ or 20, wherein said mammal is a human.